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Patrick MANSON & G.C.LOW

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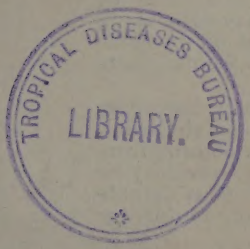
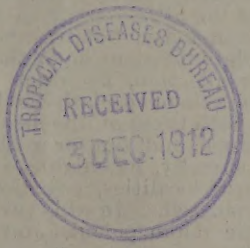




THE LEISHMAN-DONOVAN BODY AND TROPICAL SPLENOMEGALY.

BY

SIR PATRICK MANSON, K.C.M.G., M.D., F.R.S., and GEORGE C. LOW, M.B., C.M.,

London School of Tropical Medicine.

THE great majority of the cases of splenic enlargement which every year return to Europe from India, Africa, and other tropical countries are undoubtedly of malarial origin. Their histories, their liability to intercurrent acute malarial phenomena, the presence in the blood during these acute attacks of the malarial parasite, and their response to quinine prove this. But over and above these malarial cases and those of leucocythaemia, cirrhosis of the liver and other well-recognized pathological conditions associated with enlargement of the spleen, there is a considerable residuum of cases of tropical disease in which enlargement of the spleen is a prominent feature, and which hitherto have not been adequately recognized or explained.

Clinically, the cases we refer to seem to fall into two categories—the subacute and the chronic. In the more acute forms there is a history at first of a malaria-like condition with recurring attacks of high fever, which, after some months, and in spite of liberal dosing with quinine, leads to the development of a very definite cachexia. This cachexia is characterized by quotidian fever—afternoon chill followed by high temperature and profuse sweating, and terminating by the following morning in a subnormal temperature—and anaemia. Although in some instances there may be intervals of apyrexia of several weeks' duration, in others there is little variation in the quotidian recurrence of fever, which is absolutely uninfluenced by quinine. In time the spleen enlarges, the anaemia becoming intense. According to our experience the patients die in a few months. The fatal event is brought about sometimes by pure asthenia, sometimes by cerebral thrombosis, sometimes by diarrhoea, sometimes by other intercurrent disease.

The second type of febrile splenic enlargement to which we refer resembles the foregoing, only the fever is much milder,

rarely exceeding 101° F., the splenic tumour and the anaemia being less pronounced. There is, however, always a malaria-like initial stage; and, just as in the other type, this and the subsequent course of the disease are unaffected by quinine. What the ultimate fate of these more chronic cases may be we cannot say, but it seems probable that they drift along as valetudinarians until they are ultimately cut off by some other affection, to which their persistently enfeebled state renders them specially liable.

In both types of the disease the tongue is clean, the appetite good, and, but for weakness, the patient feels fairly well, Occasionally, as might be expected in persons coming from malarial localities, attacks of genuine malarial fever may be interpolated. In this event there may be considerable gastric derangement, and quinine may be of temporary service.

In certain instances the skin becomes deeply and fairly uniformly pigmented. Owing to this latter circumstance, and because most of the cases which have passed under our observation have come from Assam and the Indian Terai, we have arrived at the conclusion that the disease is none other than what is known by the natives in Assam and India as kala-azar or kala-dunkh.[1] We have seen an exactly similar condition in a patient from South Africa, but whether his case and the Indian disease are identical we are not prepared to say.

On the discovery of the trypanosoma as a factor in human pathology it occurred to us that possibly in this or a similar organism the obscure cases we have attempted to outline might receive their explanation. Accordingly in two instances of non-malarial febrile splenomegaly—one from India, one from Africa—we made careful examination of the peripheral and splenic blood, but without finding any parasite. It may be that in the Indian case our failure was attributable to the fact that the puncture in the spleen was made into sloughy and gangrenous tissue.* Notwithstanding these failures, and encouraged by Leishman's and Donovan's discovery of what appears to be a new protozoal organism in cases of the type we have described, when some time ago such a patient from the Darjeeling district consulted one of us, we persuaded him to enter the tropical wards of the Seamen's Hospital and submit to splenic puncture. This little operation was performed on two occasions—December 18th and 28th, 1903. The first tapping was followed by a slight rise of temperature, which quickly subsided to normal; the second tapping was also followed by fever and some perisplenitis.

At the first tapping we got very little blood, barely enough to fill the needle of the exploring syringe; at the second tapping quite a drachm of blood was obtained. In both specimens, on submitting them to microscopical examination, we found Leishman-Donovan bodies in great profusion. They were especially numerous in the first specimen, many fields of the microscope showing dozens of them.

Although Leishman and Donovan, and latterly, working with Donovan slides, Laveran and Ross, have described them, our observations on these bodies may be of some interest and value, inasmuch as they confirm and perhaps supplement

* This case died. Smears of blood from bone marrow and spleen showed many Leishman-Donovan bodies.

the descriptions of the earlier observers, but more especially as they completely disprove Laveran's contention that the parasites are parasites of the red blood corpuscles, and a species of piroplasma. We may at once state that although parasites were frequently encountered superposed on or underlying a red corpuscle, we have not once seen anything that would lead us to believe that they were inside the corpuscle.

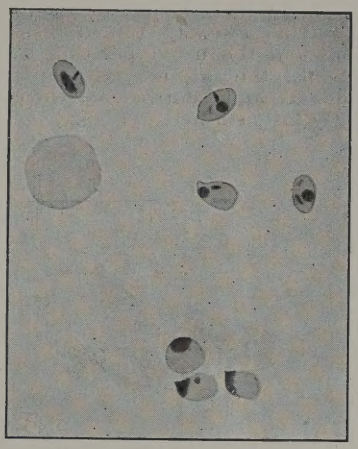


Fig. 1

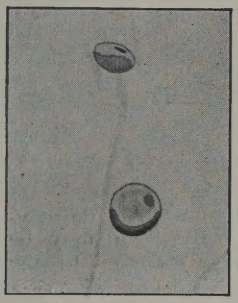


Fig. 2.

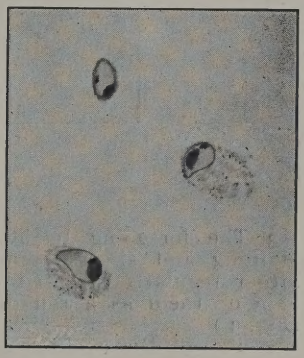


Fig. 3.

Our examinations were made in ordinary wet blood preparations, in hanging-drop preparations, and in dried and stained films. The stains employed were the Leishman-Romanowsky carbol-fuchsin and carbol-thionin; fuchsin was a failure. The Romanowsky stain gave by far the best results.

In the stained films we recognized the following:

1. Oat-shaped, oval, and circular bodies, clearly defined in outline, stained a faint blue, and having a rather large and deeply-stained usually spherical nucleus lying against the

capsule about the middle of the parasite, and a still more deeply-stained, short, bacillus-like body on the opposite side of the capsule, but directed as a rule, but not invariably, towards the nucleus at various angles. In a few instances this bacillus-like centrosome, if so we may call it, is represented by a point. The centrosome is stained even more darkly than the nucleus, which, when large, is distinctly less deeply coloured. (Fig. 1.)

2. Similar and generally rather larger bodies with the nucleus (*a*) larger and less deeply stained, or (*b*) with the nucleus spread out as a deeply-stained layer on the inside of the capsule, and in the usual position this is *vis-a-vis* to the centrosome. In the latter type of parasite, with the exception of nucleus and centrosome, the contents of the capsule are very faintly stained. (Fig. 2.)

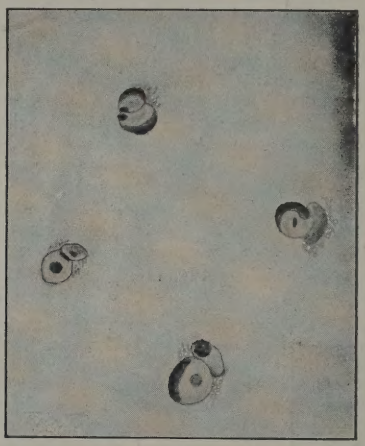


Fig. 4.

3. The foregoing bodies in association with a faintly-staining and slightly granular substance, which may be either regularly disposed around them or attached to one side of them as a roundish or flocculent irregular mass. (Fig. 3.)

4. Two of the oval bodies closely applied to each other, one of the bodies being usually smaller than the other. Occasionally in these twin bodies their respective nuclei and centrosomes are disposed symmetrically. (Fig. 4.)

5. Two or more up to fifty of these bodies arranged as an almost perfectly circular sharply-defined rosette, the matrix of the zoogloea mass being evidently of the same nature as the faintly-staining material already referred to as being sometimes attached to the single isolated parasites. These rosette-like bodies, when made up of eight or ten elements, but for the presence of the centrosomes could easily be mistaken for a sporulating quartan fever rosette. The parasites

composing the smaller rosettes are usually larger than those in the bigger groups. (Fig. 5.)

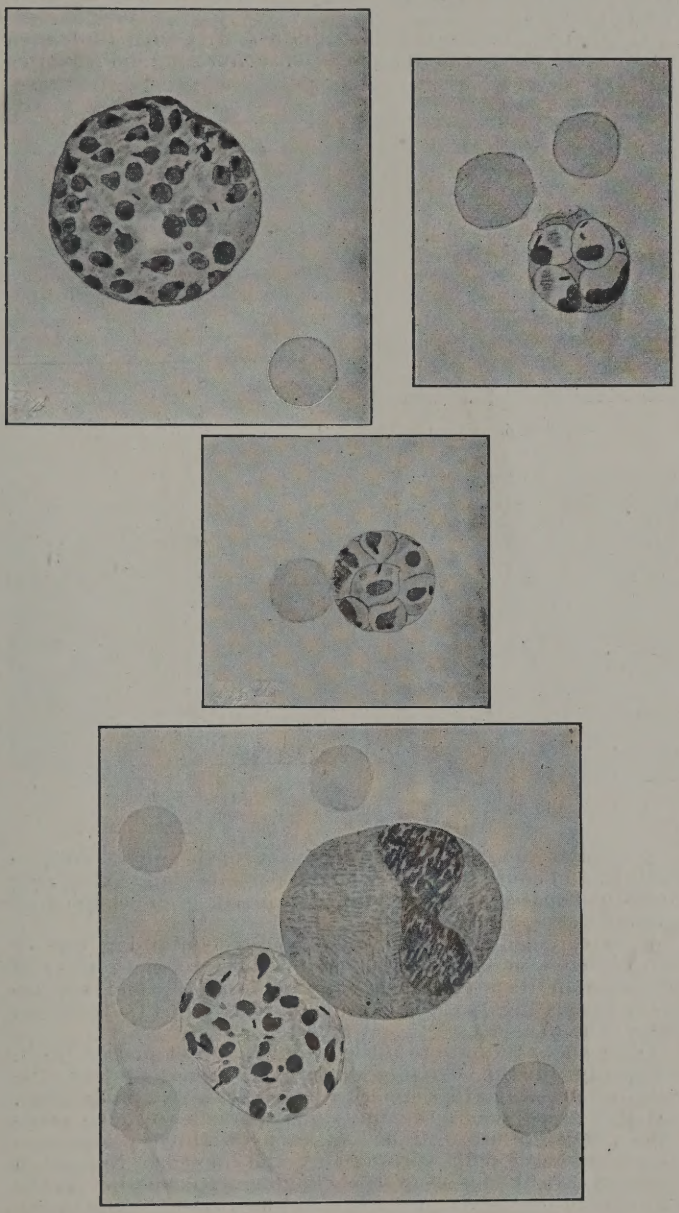


Fig. 5.

6. The same zoogloea masses broken up evidently in making the preparation, the parasites and matrix being scattered about irregularly but still keeping more or less in association (Fig. 6).

7. Circular masses of the zoogloea matrix with ill-defined outline and varying in diameter, but containing no parasites (Fig. 7).

Fig. 6.

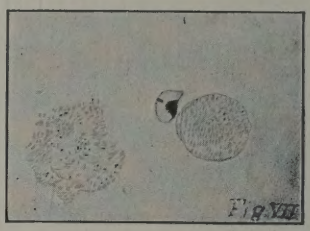


Fig 7.

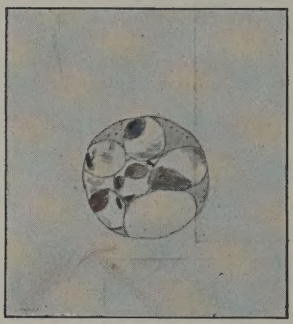


Fig. 8.

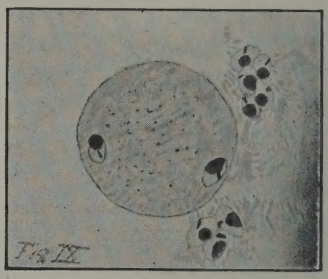


Fig. 9.

8. Similar and generally larger masses with more definite outline, and containing one or more parasites, and exhibiting unstained spaces which may have formerly been occupied by parasites (Fig. 8).

9. Sharply-defined capsule-like bodies containing one or two parasites or quite empty, but with a zoogloea mass of parasites in its neighbourhood, the proximity and appearances suggesting that the capsule had contained the zoogloea mass (Fig. 9).

From an examination of the parasite in wet preparations, especially in the hanging drop, it is apparent that the zoogloea masses have a spherical mulberry-like arrangement. In such preparations the individual parasites can be made out as very minute oval bodies, each of which possesses a highly refractile point, presumably the nucleus. Neither in ordinary wet films, nor in the hanging drop, whether on the ordinary or on the warm stage, could we make out any movement or indication of growth or development.

The evidence of phagocytosis is difficult to assess, seeing that it is always possible that in preparations in which the parasites are very abundant the appearance of inclusion of a parasite by a white blood corpuscle may be owing to superposition. However, in the case of the macrophage represented in Fig. 10 there can be no question of superposition; the parasites in this phagocyte were too numerous to admit of such an explanation.

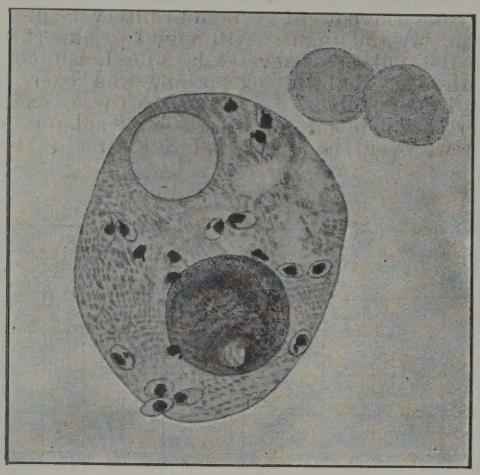


Fig. 10.

Fig. 11.

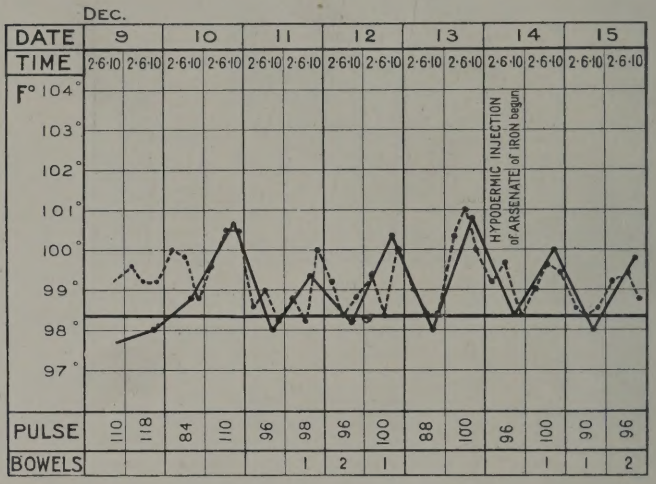
[*Magnification of figures circa* 1500]

There can be little doubt, from the frequency with which Donovan has found it in India, and of the occurrence of chronic febrile splenomegaly in Europeans from India and possibly elsewhere, that this new parasite is one to be reckoned with in tropical pathology. It would be important therefore to follow out its life-history, and more especially to be able to determine how it obtains entrance into the human body.

Judging from the appearances met with in our preparations, it seems fairly safe to assume that once in the spleen it multiplies by simple division. Certain of the parasites, after being liberated from the zoogloea masses, are destined

for passage into another phase outside the body, others for endogenous multiplication. The latter on becoming free in the splenic pulp probably conjugate, and throw out a material which ultimately forms the matrix of the zoogloea masses within which the parasites divide for some five or six generations. This goes on indefinitely apparently.

Thinking that the blood might be the medium by which the parasite travels towards its exogenous phase, we made repeated and prolonged examinations of peripheral blood obtained from the patient at regular intervals of two hours during the day and night. Although two expert assistants worked at these films for several days no Leishman-Donovan body, with one doubtful exception, was ever found by them or by ourselves. Neither in these examinations of the peripheral blood nor in those of splenic or hepatic blood did we ever encounter malarial parasites or malarial melanin.



It is evident that the parasite must get out of the body somehow, and that the blood is the most probable channel. We thought that possibly the parasite was filtered out from the splenic blood as the latter passes through the liver in the portal circulation. Accordingly we tapped our patient's liver, and found in the small quantity of blood so obtained numerous single or double parasites but no zoogloea masses. This discovery seemed to point to the biliary ducts as the channel through which the parasites escaped to gain subsequent freedom by passing out of the body with the faeces, but repeated examinations of the faeces were negative. Similarly, centrifuged urine also yielded no parasites. A curious feature about the parasites from the liver was that in quite 90 per cent. of them the nucleus was either extruded and swollen, or was in process of extrusion (Fig. 11). Possibly this phenomenon was owing to the blood having been diluted with normal salt solution. An attempt to cultivate the parasites in blood agar failed.

The following are the leading facts of the case:

C. O., aged 37, a tea-planter, when 10 years of age had Pott's disease of the lower dorsal vertebrae, which has eventuated in permanent kyphosis. He is delicate looking, but had good health till 1897. From 1893 to 1897 he was in Assam; in the latter year he went to Sylhet, where he got severe bilious remittent fever. He was in the Dooars from 1898 to 1899, and did not have much fever; again in Sylhet, in 1900, but this time he had little fever. He came home in 1901. From January, 1902, to June, 1903, he was in the Terai, near Darjeeling, and had at first good health, but in June last he began to get low fever, and in July had two sharp attacks, for which he was sent to the hills. He improved a little, but, returning to work in August, he became subject to regular tertian (as he calls them) attacks. Getting steadily worse, he was sent to the hills again on August 18th; there he got double pneumonia. On October 8th he was invalided, arriving in London on November 13th. During the first part of the voyage he felt better, but later he got fever every afternoon, followed by profuse night sweats. Since his arrival in England he has had fever every third day, with occasional but milder intervening attacks. He has been taking quinine steadily for months without apparent benefit. On November 30th, 1903, it was found that his spleen came $3\frac{1}{2}$ in. below the costal border, was smooth and firm. His liver was also enlarged, the free edge coming well below the costal border. The urine had about a-sixth of albumen. Lungs and heart were normal. Blood contained no malarial parasites, and the red corpuscles were regular in size, 3,600,000 per c.mm. He was admitted into the tropical wards of the Seamen's Hospital, Albert Docks, on December 6th, and has been there ever since. For a few days at a time his temperature has been normal. Most days there has been an evening rise to 99.5° or 100°. On the day on which the spleen was first tapped it stood at 102.6°, after the second tapping the temperature got as high as 103°, but in three days with the decline of the perisplenitis it fell to normal. His tongue has been clean throughout, and his appetite fair. The urine is now free from albumen.

The blood count was as follows:

Blood Counts.

	December 17th.	December 18th.*	December 30th.†
Red cells	3,500,000	3,650,000	4,000,000
White cells	3,700	3,100	3,120
Haemoglobin	56%	57%	64.0%
Polymorphonuclear ...	40%	42%	44.0%
Large mononuclear ...	13%	11%	10.5%
Lymphocytes	44%	41%	40.8%
Eosinophiles	2%	2%	1.1%
Transitional	-	1%	2.1%
Mast cells	1%	3%	0.6%
Malaria parasites ...	*Nil*	*Nil*	*Nil*

* Spleen punctured. † Spleen and liver punctured.

We are very much indebted to Dr. T. S. Kerr for the extremely accurate drawings which illustrate this paper.

REFERENCE.

1 *Tropical Diseases*, 3rd edition, p. 271.

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